



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/439,594	11/12/99	RABBANI	E ENZ-58 (DIV1)

RONALD C FEDUS ESQ
ENZO DIAGNOSTICS INC
C/O ENZO BIOCHEM INC
527 MADISON AVENUE 9TH FLOOR
NEW YORK NY 10022

HM22/1220

EXAMINER

TUNG, J

ART UNIT

PAPER NUMBER

1656

DATE MAILED:

12/20/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/439,594

Applicant(s)

Rabbant et al.

Examiner
Joyce Tung

Group Art Unit
1656



- ☐ Responsive to communication(s) filed on _____
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 60-145 is/are pending in the application.
- Of the above, claim(s) 74-145 is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 60-73 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☒ Claims 60-145 are subject to restriction or election requirement.

Application Papers

- ☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of References Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☒ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Art Unit: 1656

DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1656.

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 60-73, drawn to a process for detecting a specific target nucleic acid involving a first or second initial primer or first or second nucleic acid constructs comprising two segments which are capable of forming a stem-loop structure for the detection, classified in class 435, subclass 91.2.
 - II. Claims 74-85 and 107-118, drawn to a process for amplifying a specific target nucleic acid involving the first and second initial primers or nucleic acid constructs which are capable of forming a stem-loop structure, but synthesizing the copies from the target is carried out under isothermal condition, classified in class 435, subclass 91.2.
 - III. Claims 86-106 and 119-126, drawn to a process for detecting a specific target nucleic acid involving the first and second initial primers or nucleic acid constructs which are capable of forming a stem-loop structure, but the first initial primers or first nucleic acid constructs or the second initial primers or constructs or both

Art Unit: 1656

converted into a form capable of stem-loop formation under isothermal condition by the presence of the specific target nucleic acid sequence, classified in class 435, subclass 91.2.

IV. Claims 127-145, drawn to a composition comprising primers or nucleic acid construct, classified in class 536, subclass 24.3/25.32.

2. Inventions IV and I-III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant the product in claims 127-145 can be used in nucleic acid purification, while the method of Groups I-III can be carried out with another nucleic acid primer, for example, the extender probe and polynucleotide primer used in the method of Western et al. (See section 11).

3. Inventions I, II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant Group I, claims 60-73 are drawn to the method for a process for detecting a specific target nucleic acid involving a first or second initial primer or first or second nucleic acid constructs comprising two segments in which the second segment of either the first primer or the second primer can form step-loop structure with the sequence that are extended by either the first segment of the first initial primer

Art Unit: 1656

or the first segment of the second initial primer, Group II is drawn to a process for amplifying a specific target nucleic acid involving the first and second initial primers or nucleic acid constructs which are capable of forming a stem-loop structure, but synthesizing the copies from the target is carried out under isothermal condition and Group III is drawn to a process for detecting a specific target nucleic acid involving the first and second initial primers or nucleic acid constructs which are capable of forming a stem-loop structure, but the first initial primers or first nucleic acid constructs or the second initial primers or constructs or both converted into a form capable of stem-loop formation under isothermal condition by the presence of the specific target nucleic acid sequence. Thus, they are unrelated invention.

4. Because these inventions are distinct for the reasons given above and the search required for each group which is different, restriction for examination purposes as indicated is proper.

5. During a telephone conversation with Mr. Ronald C. Fedus on 10/24/2000 a provisional election was made with traverse to prosecute the invention of Group I, claims 60-73.

Affirmation of this election must be made by applicant in replying to this Office action. Claims 74-145 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any

Art Unit: 1656

amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

7. The title of the invention is not descriptive because the old title is directed to novel specific target nucleic acid detection and amplification processes, and compositions useful for producing one or more copies of specific target nucleic acid sequence. The language is directed to a process for detecting a target nucleic acid involving detecting the presence of the stem-loop structure formed by self-annealing between the second segment of the first initial primer and a segment derived from target template dependent extension of the first segment of the first initial primer. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Objections

8. Claims 65-66, and 71-73 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim 64, 66, and 70-71. See MPEP § 608.01(n). Accordingly, the claims 65-66, and 71-73 not been further treated on the merits.

Claim Rejections - 35 U.S.C. § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1656

10. Claims 60-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 60-73 are vague and indefinite because of the language "substantially complementary to", "substantially identically", "substantially non-identical" in claim 60 which is unclear how the language with "substantially" is defined in the specification. In addition, the language "derived from" is unclear because the segment is synthesized by the extension of the first segment of the first primer from the target nucleic acid used as a template, and the segment is not a derivative with the chemical modification of the extension of the first segment of the first primer from the target nucleic acid used as a template. It is suggested to clarify uncertainty.

b. Claims 67-73 are vague and indefinite because of the language "substantially complementary" in claim 67 which is unclear how the language with "substantially" is defined in the specification. In addition, it is unclear which template is used to synthesize the sequences that are synthesized after extension of the first initial primer and is substantially complementary to the first segment of the second primer.

c. Claims 68 and 70-73 are vague and indefinite because of the language "substantially non-identical to", "substantially identical to" and "substantially complementary to" in claims 68 which is unclear how the language with "substantially" is defined in the specification.

d. Claim 72 is vague and indefinite because it is unclear how the language "substantially completed" is defined in the specification.

Art Unit: 1656

- e. Claim 73 is vague and indefinite because it is unclear how the language "substantially completed" is defined in the specification. In addition, it is unclear how the detection is done by detecting the formation of a stem-loop structure which takes place before nucleic acid synthesis because as set forth in claim 60 the stem-loop structure is formed by self-annealing between the second segment of the first initial primer and a segment synthesized from the target used as template by the template dependent extension of the first segment of the first initial primer. It is suggested to clarify uncertainty.
- f. Claims 67-73 are vague and indefinite because it is unclear how the second initial primer is involved in the detection of the specific target nucleic acid sequence with the detection of the presence of the stem-loop structure.
- g. Claim 66 and 72-73 are vague and indefinite because it is unclear how the detection is taken place without the amplification of the target nucleic acid.
- h. Claims 60-73 are vague and indefinite because it is unclear without a denaturation step how the first segment of the first initial primer is extended and the stem-loop structure is detected. It might mean that the process is one single cycle amplification. It is suggested to clarify uncertainty.

Claim Rejections - 35 U.S.C. § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1656

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 60-65, and 67-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Western et al. (5,612,199).

Western et al. disclose that a method of detecting the presence of a nucleic acid analyte by examining the presence of the extended primer (See column 6, lines 45-49 and column 7, lines 17). The method allows extension of an extended probe along a single stranded target sequence to produce a single stranded sequence having the capability of forming an intramolecularly based paired structure in which the 3' end not involved in the production is modified (See column 7, lines 55-64). The extended probe comprises the sequence EP1 at 3' end which is hybridized to the S1 sequence of the analyte and the other sequence EP2 is substantially identical to S2 sequence of the analyte and not complementary to the analyte (See column 6, lines 46-68). A polydeoxynucleotide primer hybridizes to a nucleotide sequence complementary to S2 (See

Art Unit: 1656

column 6, lines 46-68). The method also involves polymerase (See column 12, lines 37) and deoxynucleoside triphosphate as needed for the amplification reaction (See column 7, lines 1-5). The disclosure indicates that there is no means for degrading the extender probe to form the polynucleotide (See column 6, lines 66 to column 7, line 1). The target sequence identified within the analyte has S1 and S2, and S1 and S2 are separated by at least ten bases, preferably at least 100, usually 200-10,000 (See column 11, lines 24-28). The extender probe is extended along the target sequence and the extended sequence forms a stem-loop structure (See column 14, lines 36-40). The label or reporter group is bound to a nucleic acid probe or primer for detection (See column 16, lines 10-36). The polydeoxynucleotide primer is single stranded containing 3' end hybridized to the complementary sequence of S2 sequence (See column 11, lines 66-68 to column 12, lines 1-4) and can be extended along the extended extender probe to form a duplex comprising the extended primer (See column 14, lines 24-32). This suggests that the extended primer can also have the structure to form a stem-loop which has the same function as the second initial primer since the extended extender probe which can form a stem-loop structure is complementary to the extended polydeoxynucleotide primer (See column 7, lines 55-64). Extension in this fashion provides the requisite fidelity between the extended primer and the polynucleotide so that accurate detection of target analytes can be achieved (See column 14, lines 32-34).

Western et al. do not disclose the polydeoxynucleotide which can be used as an second initial primer. However, the primer used for the second round amplification has the same function

Art Unit: 1656

as the second initial primer as claimed because both are polynucleotide and have two segments, for example, first segment is complementary to sequence that are synthesized after extension of the extender probe.

The teachings of Western et al. suggest the limitations of claims 60-65, and 67-72. Instant claims 60-65, and 67-72 are drawn to a process of detecting the presence of a specific target nucleic acid sequence involving two initial primers. The first initial primers comprise two segments in which the first segment is complementary to a portion of the specific target nucleic acid and capable of template extension and the second segment is non-identical to the first segment, identical to a portion of the specific target nucleic acid and complementary to the sequence that are synthesized by extension of the first segment of the first initial primer. The second initial primer comprises the same structure as the first initial primer. The detection is done by the presence of the stem-loop structure by self-annealing between the second segment of the first initial primer and the segment synthesized from the extension of the first segment. The process also involves nucleic acid polymerase as listed in claim 61, the detectably labeled primers in which the moieties and labels are listed in claims 62-64 and 69-71.

One of ordinary skill in the art would have been motivated to use the method of Western et al. because the method of Western et al. is used for detecting the presence of a polynucleotide analyte in a sample by examining the presence of the extended primer (See column 6, lines 5-67 to column 7, lines 1-17) in which the produced single stranded polynucleotide can have an intramolecularly base-paired structure and 3' end of the extender probe is modified and the

Art Unit: 1656

method provides a highly convenient method for converting a polynucleotide sequence of interest to a target sequence having an intramolecularly base-paired structure while minimizing the number of reagents and steps required (See column 7, lines 55-67 and column 8, lines 1-6). In addition, extension of the polydeoxynucleotide primer provides the requisite fidelity between the extended primer and the polynucleotide so that accurate detection of target analytes can be achieved (See column 14, lines 32-34). Thus, an artisan of ordinary skill in the art based upon the teachings of Western et al. would have made the instant invention as claimed. It would have been prima facie obvious to carry out the process as claimed.

13. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Margaret Parr can be reached at (703) 308-2454.

14. Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1656 via the PTO Fax Center located in Crystal

Application/Control Number: 09/439,594

Page 12

Art Unit: 1656

Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

Joyce Tung
December 4, 2000

A handwritten signature in cursive script that reads "Eggerton Campbell". The signature is written in dark ink and is positioned above the printed name and title.

**EGGERTON A. CAMPBELL
PRIMARY EXAMINER**